lines 1-5. Claim 44 has been amended to provide for proper antecedent basis. A copy of all of the pending claims as they are believed to have been amended is attached to this amendment as an appendix.

The present invention is directed to CTL recognized peptide epitopes. The claimed peptides are processed so that a fragment (at least the minimal sequence recognized by the CTL) is produced which is able to bind to an appropriate MHC molecule and be presented by a cell to elicit a suitable T cell response.

Rejection Under 35 U.S.C. § 112, first paragraph

Claims 1, 4-6, 15 and 19 were rejected under 35 U.S.C. § 112, first paragraph, as not being enabled. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

Claim 1 has been amended to include only those peptides that either bind to HLA-A0201; or are capable of being processed by an APC to form a polypeptide that binds to HLA-A0201. Therefore, claim 1 is clearly directed to polypeptides that result in the presentation of the RMFPNAPYL polypeptide motif on the surface of a cell that expresses HLA-A0201. Claim 19 is limited to a vaccine for a cancer that is HLA-A0201 positive and over expresses WT-1. The examiner has already indicated (see page 3, third paragraph, of Office Action mailed on May 20, 2002) that the present specification provides sufficient guidance for vaccines that over express WT-1 and express HLA-A2.

Claims 1, 4-6, 15 and 19 were rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor had possession of the claimed invention. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

The examiner rejected claims 1, 4-6, 15 and 19 on the basis that "there is insufficient written description for a peptide able to bind class I molecules which comprises at least 6 consecutive residues of SEQ ID NO:1.....". The claims have been amended to delete reference to peptides comprising at least six consecutive amino acids of SEQ ID NO:1.

Claims 43-48 were rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor had possession of the claimed invention. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

The Legal Standard.

The first paragraph of 35 U.S.C. § 112 sets forth the written description requirement for patents as follows:

> "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains or with which it is most nearly connected, to make and use the same,

and shall set forth the best mode contemplated by the inventor of carrying out his invention."

The standard regarding what is or is not supported by the specification has been clearly articulated as requiring the specification to convey with reasonable clarity to those skilled in the art that, as of the filing date sought, the inventor was in possession of the invention, i.e., whatever is now claimed. *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555 19 USPQ2d 1111, 1117 (Fed . Cir. 1991). Compliance with the written description requirement is essentially a fact-based inquiry that will "necessarily vary depending on the nature of the invention claimed." *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563 (Fed. Cir. 1991) (citing *In re DiLeone*, 436 F.2d 1404, 1405 (CCPA 1971)). Essentially, satisfaction of the written description requirement is determined on a case-by-case basis.

The inquiry into adequate written description is not performed in a vacuum. "Knowledge of one skilled in the art is relevant to meeting [the written description] requirement." *Enzo Biochem, Inc. v. Gen-Probe*, Docket No. 01-1230 (Fed. Cir. Apr. 2, 2002) (slip op.). This fact has implications not only for validity challenges, but also for patent prosecution. *See In re Alton*, 76 F.3d 1168, 1174-75 (Fed. Cir. 1996).

The Examiner asserts that the instant disclosure of a peptide comprising the amino acid sequence of SEQ ID NO:1 does not adequately describe the scope of the claimed genus. This rejection appears to be directed to claim 1. The term "comprising" in the instant claims does not refer to an indeterminate number and type of amino acids. Claim 1 is directed to a peptide

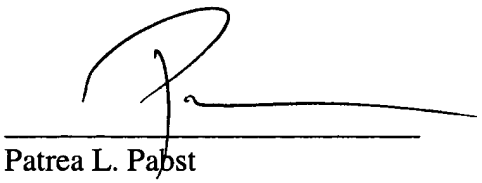
having at least 9 but fewer than 100 amino acids, thereby defining the number of amino acids in the peptide. Furthermore, the peptide is capable of either binding to HLA-A0201, or being processed by an antigen presenting cell so that a fragment is produced which is able to bind to HLA-A0201. The identity of the sequences that flank the SEQ ID NO:1 motif is not important to the correct processing of the polypeptide. An APC is able to correctly process virtually all proteins it is exposed to. Again, in view of the Janeway publication, the Applicants have submitted that current evidence suggests that N-terminal trimming of peptide fragments occurs within the endoplasmic reticulum of an APC. This is the site where a C-terminal trimmed peptide binds to an MHC class I molecule. The protruding N-terminal is then trimmed back by an aminopeptidase to produce a molecule that is of the correct size to best fit the MHC's peptide binding groove (see enclosed Shastri reference, at page 483, lines 16-17):

"these studies provide compelling arguments for aminopeptidase trimming in the ER as a key event in the antigen processing pathway".

In view of the foregoing discussion, as it relates to claim 1, claim 44 finds more than adequate support in the specification as originally filed, in combination with what is generally known in the art.

Allowance of claims 1, 5, 7, 15, 19, and 44 is respectfully solicited.

Respectfully submitted,



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Date: November 7, 2002

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Certificate of Mailing Under 37 C.F.R. § 1.8(a)

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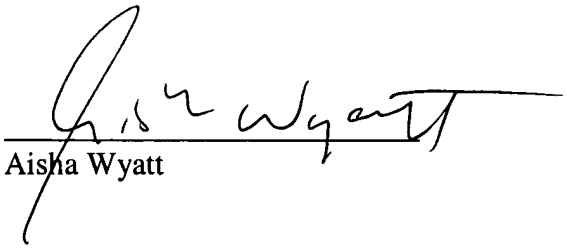

Aisha Wyatt

Date: November 7, 2002

Marked Up Version of Amended Claims
Pursuant to 37 C.F.R. § 1.121(c)(1)(ii)

1. (Four times amended) A peptide having at least [8] 9 but fewer than 100 amino acids, which peptide comprises [an] the amino acid sequence [selected from the group consisting of] RMFPNAPYL (SEQ ID NO:1) [; a peptide comprising at least six consecutive amino acids of SEQ ID NO:1, and variants thereof wherein the side chains of one or two to the amino acids of SEQ ID NO:1 are altered], and wherein the peptide is capable of:

(a) binding to HLA-A0201; or

(b) being processed by an antigen presenting cell so that a fragment is produced which is able to bind to HLA-A0201.

Please cancel claim 4.

5. (Amended) A peptide according to claim [4] 1 wherein the peptide is capable of binding to HLA-A0201 and, when bound to HLA-A0201, the peptide-bound HLA-A0201 is capable of eliciting the production of a cytotoxic T lymphocyte (CTL) which recognises a cell which aberrantly expresses a polypeptide comprising the given amino acid sequence.

Please cancel claim 6.

7. (Three times Amended) A peptide according to claim 1 consisting of the amino acid sequence RMFPNAPYL (SEQ ID NO:1).

15. (Twice Amended) A pharmaceutical composition comprising the peptide of Claim 1 and a pharmaceutically acceptable carrier.

19. (Three times Amended) A vaccine for a tumor cell in which HLA-A0201 is expressed and WT-1 is over expressed, the vaccine comprising a peptide according to claim 1 [cancer in which WT-1 is aberrantly expressed comprising a peptide having at least 8 but fewer than 100 amino acids, which peptide comprises an amino acid sequence selected from the group consisting of RMFPNAPYL (SEQ ID NO:1); a peptide comprising at least six consecutive amino acids of SEQ ID NO:1; and variants thereof wherein the side chains of one or two of the amino acids of SEQ ID NO:1 are altered].

Please cancel claim 43.

44. (Amended) The peptide of claim 1 consisting of from [8] 9 to 12 amino acids.

Please cancel claims 45-48.